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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,606	05/05/2005	Maria Cristina Geroni	17703 (PC27210A)	4724

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EXAMINER	
WEBB, WALTER E	

ART UNIT	PAPER NUMBER
1614	

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12/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,606	GERONI ET AL.	
	Examiner	Art Unit	
	Walter E. Webb	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-11,13-15 and 24-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-11,13-15 and 24-30* is/are rejected.

7)☒ Claim(s) *7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 1-3, 5-11, 13-15 and 24-30 are pending and rejected.

Claim 4, 12, and 16-23 have been cancelled.

Response to Amendments

The § 101 and § 112, second paragraph rejection with regard to claims 16-23 are withdrawn since these claims have been deleted.

The § 112 second paragraph rejection with regard to claims 1-9 reciting "distamycin or distamycin-like frame work" is withdrawn since that phrase has been deleted from those claims.

Claim Objections

Claim 7 is objected to because of the following informalities: The use of periods to number the compounds of the Markush group. MPEP § 608.01(m) states that "[p]eriods may not be used elsewhere in the claims except for abbreviations." Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims 9-11, and 13-14 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant argues that the term "combined preparation" means the treatment is staged, rather than combining the two drugs into one drug. However, this is ineffective to overcome the rejection. Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term "combined preparation" in claim 9 is used by the claim to mean a staged treatment regimen, while the accepted meaning is a medicinal substance together, not separate. The product clearly requires the elements to be together, and thus does not allow for anything but simultaneous administration. The term is indefinite because the specification does not clearly redefine the term.

Claim Rejections - 35 USC § 103

Claims 1-27 were rejected under 35 U.S.C. 103(a) as being unpatentable over Cozzi et al. (WO 98/04524, published February 5, 1998) in view of Sironak et al., (Clinical Cancer Research: 2000, 6 (12); 4885-4892) and further in view of Grimley et al., (US 6,274,576). This rejection is maintained and is now applicable to claims 1-3, 5-11, 13-15 and 24-30.

Applicant amended claim 1 to include the term "having a synergistic antineoplastic effect" and argues that this amendment renders the claim no longer obvious of the cited references, since those references, either alone or in combination, do not teach the claimed composition. Applicant also submits Exhibit 1, which applicant argues supports the synergistic effect of combining a compound of formula I with STI571. This is found to be unpersuasive for several reasons. First, with respect to the composition (claims 1-3, 5-11, and 13-15), unexpected results would not overcome the motivation to combine a compound of the Cozzi with the protein kinase inhibitor of Sirotnak. Applicant has disclosed *in vitro* data (Exhibit I) combining one compound of formula I (Brostallicin) with three protein kinase inhibitors to support their claim of unexpected results, while claims 24, 26 and 28-30 broadly claim a synergistic antineoplastic effect with any compound of formula I and any protein kinase inhibitor *in vivo*. Even if each of the examples provided showed the presence of an unexpected result, those examples would not provide an adequate basis for concluding that the great number of composition recited in generic claims 24, 24, and 28-30 would behave in the same way. Second, a person having ordinary skill in the art would reasonably expect a synergistic effect in combining these compounds, which are known in the art for treating the same disease. With respect to synergism and unexpected results, MPEP § 716.02(a) states, "A greater than expected result is an evidentiary factor pertinent to the legal conclusion of obviousness ... of the claims at issue." In re Corkill, 711 F.2d 1496, 226 USPQ 1005 (Fed. Cir. 1985). Evidence of a greater than expected result may also be shown by demonstrating an effect which is greater than the sum of

each of the effects taken separately (i.e., demonstrating "synergism"). *Merck & Co. Inc. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), *cert. denied.* 493 U.S. 975 (1989). However, A synergistic effect is not necessarily sufficient to overcome a prima facie case of obviousness if such an effect is expected. Applicants must further show that the results were greater than those that would have been expected from the prior art to an unobvious extent, and that the results are of a significant, practical advantage. Ex parte The NutraSweet Co., 19 USPQ2d 1586 (Bd. Pat. App. & Inter. 1991) (Evidence showing greater than additive sweetness resulting from the claimed mixture of saccharin and L-aspartyl-L-phenylalanine was not sufficient to outweigh the evidence of obviousness because the teachings of the prior art lead to a general expectation of greater than additive sweetening effects when using mixtures of synthetic sweeteners.)

Furthermore, a person of ordinary skill in the art would reasonably expect a synergistic effect in light of the fact that Sirotnak et al. teach that the coadministration of a protein kinase inhibitor (ZD1839) will **enhance** the efficacy of cytotoxic agents, and demonstrates a more than additive effect when coadministered with a known cyotoxic agent. While it is true that Sirotnak does not use the same cytotoxic agent as in the instant application, the artisan would reasonably expect success with coadministration of applicant's cytotoxic agent given that the various cytotoxic agents tested in the reference had "highly diverse mechanisms of action." (See Discussion at pg. 4890, right col., third paragraph.) The synergistic effect of ZD1839 coadministered with a cytotoxic agent can be seen in Fig 5 at pg. 4890 of Sirotnak.

Applicant also argues that there are several differences between the composition in Cozzi et al., and that of the present invention. (See Remarks at pg. 13.) This is found to be unpersuasive since the limitiations for Cozzi and the instant formula remain the same. For example, R1 and R2 of Cozzi can be hydrogen, the instant application replaces R1 and R2 with hydrogen. The limitations of Cozzi are broader, but still anticipate the acryloyl distamycin derivative of the instant application.

Applicant argues that because the compounds of Sironak et al., and Grimley et al. are structurally and functionally different from the distamycin derivatives of the instant application, a person of ordinary skill in the art would not combine teachings of these two references with Cozzi. The examiner disagrees. The fact that the compounds in question treat the same disease establishes prima facie obviousness in combining them to form a third composition for treating the same disease. "The question under 35 USC 103 is not merely what the references expressly teach but what they would have suggested to one of ordinary skill in the art at the time the invention was made." *In re Lamberti* , 545 F.2d at 750, 192 USPQ at 280.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir.

1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-27 were rejected on the ground of nonstatutory obvious-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 6,482,920 (Cozzi) in view of Sirotnak et al., (Clinical Cancer Research: 2000, 6 (12); 4885-4892). This rejection is maintained and is now applicable to claims 1-3, 5-11, 13-15 and 24-30.

Applicant makes the same argument above with regard to this obvious-type double patenting rejection.

For the reasons stated above in the 35 USC § 103(a) rejection, the rejection under the obvious-type double patenting is also maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Walter E. Webb whose telephone number is (571) 270-3287. The examiner can normally be reached on 8:00am-4:00pm Mon-Fri EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

WW

Frederick Krass
Primary Examiner
Art Unit 1614